Evaluation of compounds on CA1 neurons spontaneous firing recorded with the MEA technique

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Material & Methods

Preparation of acute rat hippocampal slices

Experiments are carried out with Sprague Dawleys rats between 3 and 4 weeks of age provided by Elevage Janvier.

Hippocampal slices (350 µm thickness) are cut with a vibratome (Leica VT1200S) in a ice-cold oxygenated sucrose solution (Saccharose 250, Glucose 11, $NaHCO_3$ 26, KCl 2, NaH_2PO_4 1.2, $MgCl_2$ 7 and $CaCl_2$ 0.5 in mM).

Then, slices are incubated at room temperature for at least 1h in ACSF of the following composition: Glucose 11, $NaHCO_3$ 25, NaCl 126, KCl 3.5, NaH_2PO_4 1.2, $MgCl_2$ 1.3, $CaCl_2$ 2 in mM.

Slice perfusion and temperature control

During experiments, the slices are continuously perfused with the ACSF (same composition as above except for KCl (5 mM), bubbled with 95%O_2–5% CO_2) at the rate of 3 mL/min with a peristaltic pump (MEA chamber volume: ~1 mL). Complete solution exchange in the MEA chamber is achieved 20 s after the switch of solutions.

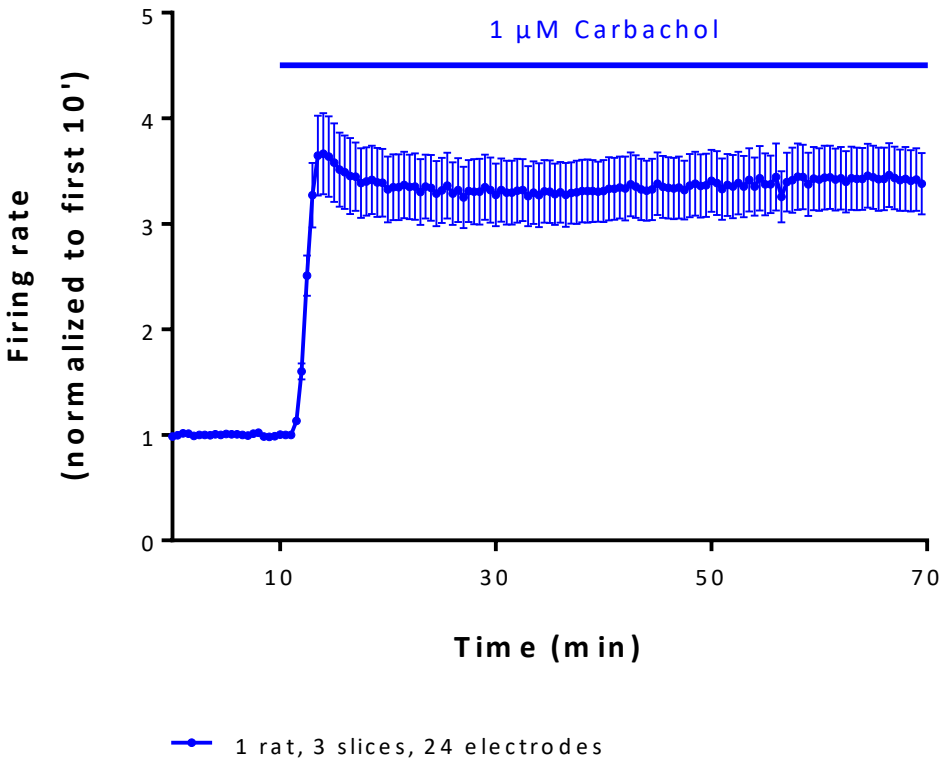
The perfusion liquid is continuously pre-heated at 37°C just before reaching the MEA chamber with a heated-perfusion cannula (PH01, MultiChannel Systems, Reutlingen, Germany). The temperature of the MEA chamber is maintained at 37 ± 0.1°C with a heating element located in the MEA amplifier headstage.

Analysis

The spikes number per second recorded at each electrode are averaged for 30 s slots and normalized to the mean spikes rate value over the control period. Individual data from independent experiments are then pooled and the mean value of the normalized spikes rate (± SEM) is plotted as a function of time (before and after exposure to the tested compound(s)).

ADVANTAGES

Stability of CA1 neurons firing rate

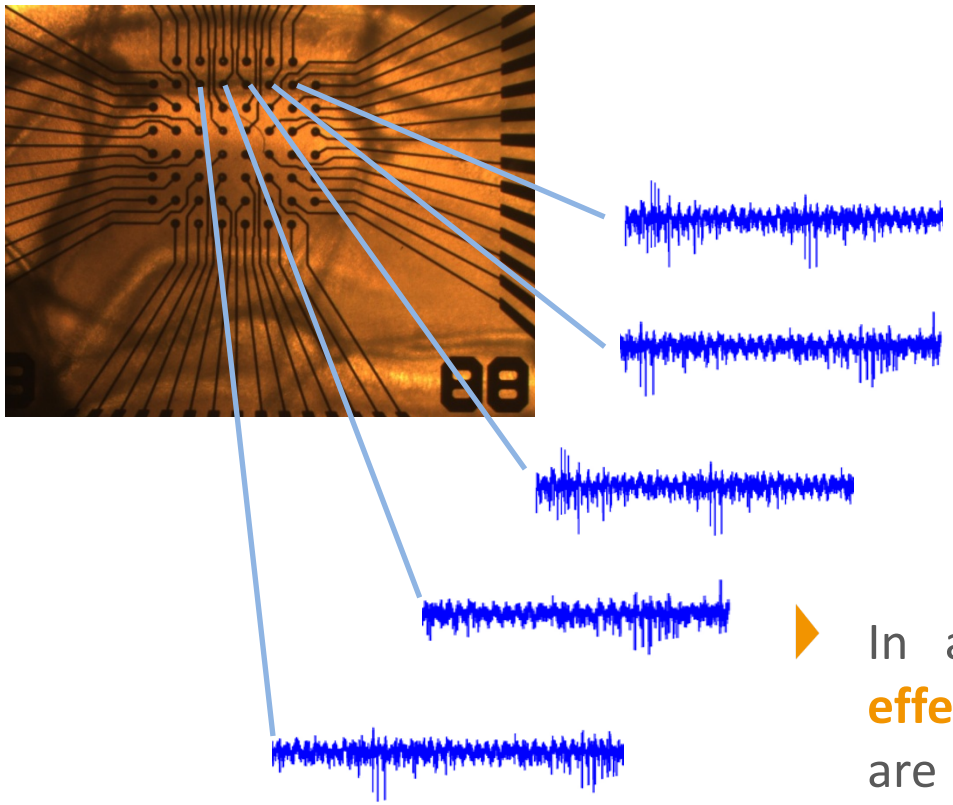


- Extracellular recording are non-invasive. In control conditions, the firing rate remains very **steady** over more than one hour. This allow to evaluate very **accurately** the compounds effect

- Example nearby: Carbachol strongly increases the firing activity. Carbachol effect stabilizes over the 10 first minutes of exposure an then remains steady untill the end of the recording session (over 50 minutes).

ADVANTAGES

Multipoints recordings

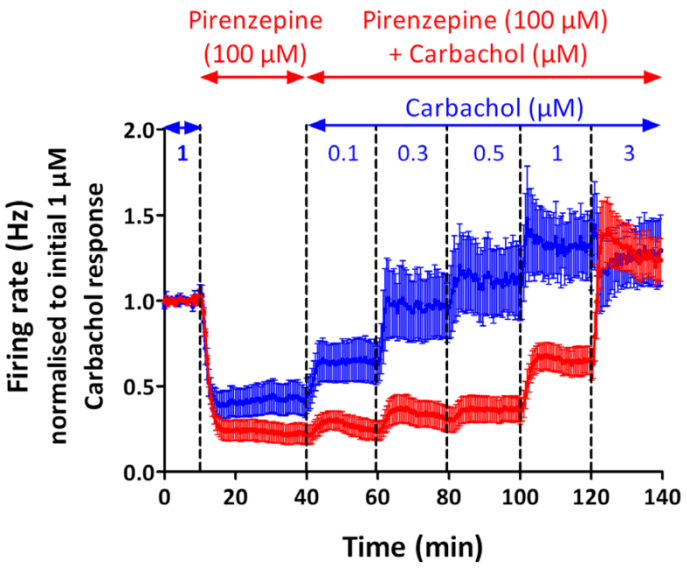


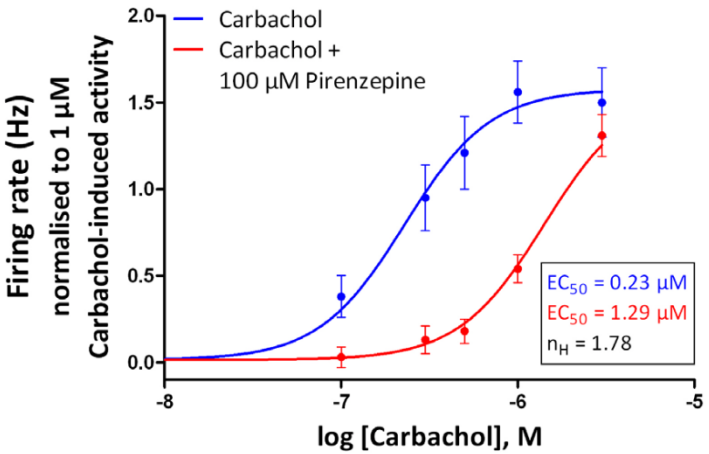
- Within each tested slice, the CA1 neurons spontaneous activity is recorded at 3 to 8 electrodes, each electrodes recording the activity of several neurons located in the vicinity. The results obtained are averaged from a large number of neurons and are then **very robust**.

- In addition, such experiments are **cost effective**: since a large number of neurons are recorded within each slice, 4 to 6 slices are enough to obtain reliable results. Several concentrations of a compound could also be evaluated on a single slice.

ADVANTAGES

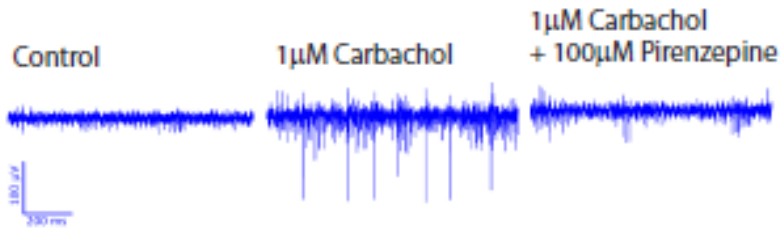
Physiological conditions





- The CA1 neurons firing activity is recorded from neurons located in a **native network**. The recording technique is **non-invasive** and the solution bathing the neurons is close to the cebebro-spinal fluid composition.

- Such experiments allow to precisely document the **pharmacological profile** of compounds, in conditions close to the *in vivo* situation.



CONCLUSION

LIMITATIONS:

- Due to the type of recording (extracellular), the MEA technique does not allow to investigate single neurons parameter such as rheobase or to apply depolarizing step to the recorded neuron.

ADVANTAGES:

- The MEA technique allows the recording a steady firing activity over a long period of time, thus providing very accurate information about the compound evaluated.
- Multipoints recordings largely increase the number of neurons recorded within a single slice and reduce the cost associated with compounds evaluation.
- Recordings are performed an environment close to the physiological conditions and allow to document the pharmacological profile of compounds.

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